

DOCKET NO.: IBIS0035-101 (IBIS-0012)  
SERIAL NO.: 09/310,667

PATENT-DRAFT  
FILED:5/12/1999

#### REMARKS/ARGUMENTS

Claims 27-29, 35-41 and 43-67 are pending and stand rejected under 35 U.S.C. § 112. Claim 51 has been amended to correct typographical errors. Claims 35, 52 and 67 have been amended. Support for this amendment can be found throughout the application as filed, including, for example, on pages 22, 24, 26, and 37-38 and Table 1 (pages 11-16). Corrected drawings were objected to as allegedly containing new matter; reconsideration of this objection is requested herein. The specification was objected to for informalities, and has been amended to correct the embedded hyperlinks and to correct the citation of a reference to which priority is claimed. Upon entry of the present amendment, claims 27-29, 35-41 and 43-67 will be pending. No new matter has been added.

#### **I. Corrections to the drawings introduce no new matter**

The corrected drawings (Figures 4 and 5A) submitted on May 1, 2003 were disapproved as allegedly introducing new matter. The Office states that "in the corrected Figure 4, there is no connection between "Annotations Relational Database" and "Filter & Sort." Applicants respectfully disagree. All changes to the Figures were made in accordance to concepts and ideas presented in correlated figures and in order to more fully and clearly describe the invention.

Figure 4 describes a flow-scheme for the QC Compare protocol which must use the Blast database and the Annotation database of Figure 3. The concept of "Annotations Relational Database" presented in Figure 4 finds support in the original disclosure at page 20, line 10, and page 21, lines 5-6. "Annotations Relational Database" also appears at the bottom of Figure 3, and it is implied that the information of Figure 4 flows from the information presented at the bottom of Figure 3 immediately preceding Figure 4; thus, Annotations Relational Database was part of the application as filed and is therefore not new matter. The informal drawing originally submitted showed a two-column format to indicate two streams of input into "Filter & Sort" where the connection between Annotations Relational Database and Filter & Sort was assumed. In the formal drawings submitted on May 1, 2003, a formal drawing was submitted for Figure 4, in which "Parsed Annotations" was amended to "Annotations Relational Database" and the

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connecting line was included in order to more particularly describe the connection between Figure 3 and Figure 4, and more particularly describe the claimed invention. Furthermore, according to Webster's Revised Unabridged Dictionary (1913), to parse means "to resolve into its elements, as a sentence, pointing out the several parts of speech, and their relation to each other by government or agreement." Therefore, Annotations Relational Database and Parsed Annotations have the same meaning in the context of Figure 4. Thus, no new matter was added to Figure 4.

The Office alleges that the added materials in Figure 5A are not supported by the original disclosure. Figure 5A is a flow chart describing the logical analysis and pathway of preferred steps in the CompareOverWins algorithm. Support for the figure as amended can be found at page 23, line 2 and in Example 2 on page 35, lines 11-15 of the original disclosure. The diamond-shaped box represents a "yes" or "no" decision point in the process, and the question asked is found within the diamond. In this context, the original phrase "Weighted Percent of Matches at better than in bestArray?" and the amended phrase "Is Weighted Percent of Matches better than Corresponding Point in bestArray?" have the same meaning and provoke the same "yes" or "no" decision. Where the correction is merely to further clarifying pre-existing text, a new matter rejection is unsupported.

Lastly, the informal drawing Figure 5A included the phrase "Set Point in bestArray to Weighted Match Percent" and this phrase was amended to "Set Point in bestArray=Weighted Match%." The Office alleges that the meanings of the two phrases are different and that the amendment introduces new matter. Applicants do not agree with the Examiner's assertion. Specifically, the phrases are written as imperative commands, where the word "to" is equivalent to "equal to" which is equivalent to the symbol "=" and the word "Percent" is equivalent to the symbol "%". Thus, the phrases have the same meaning.

In summary, the previously submitted formal drawings (Figure 4 and Figure 5A) have the same meanings as the originally submitted informal drawings. No new matter appears in these formal drawings.

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**II. Hyperlinks rejections under 35 U.S.C § 112, first paragraph**

The office has objected to the disclosure because it contains embedded hyperlink and/or other form of browser-executable code. The present specification has been amended so as to delete all hyperlink and/or other form of browser-executable code. Applicants assert therefore that these rejections are moot and request reconsideration in view thereof.

**III. Claims Are Fully Described under 35 U.S.C. § 112, first paragraph**

In the Office Action mailed July 1, 2003, claims 27-29, 35-41 and 43-67 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Applicants disagree and respectfully traverse the rejection.

Applicants had possession of the claimed invention at the time the application was filed, and the present application fully describes and teaches the skilled artisan how to make and use the claimed invention. Applicants' invention is directed to the genus of "oligonucleotides comprising a molecular interaction site present in the RNA of a selected organism, and in the RNA of at least one additional organism wherein the molecular interaction site serves as a binding site for at least one molecule which, when bound to the molecular interaction site, modulates the expression of the RNA in the selected organism" (original specification, page 4, lines 6-10). The Office alleges that "Since independent claims 35, 51, 52, and 67 are directed to a product and are not directed to a method and it is well established that the determination of the patentability of the product is based on the product itself and is not dependent on the method for identifying the product, the method as recited in claims 35, 51, 52 and 67 is not read into the claims." (Office Action, July 1, 2003, page 6, lines 5-8). Applicants agree that the invention is the product and not the method; the product of the instant invention is "molecular interaction sites" identified by the described process. Applicants further note that the Revised Interim Guidelines for the Examination of Patent Applications published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp. 71427-71440, cited by the Examiner (Office Action, July 1, 2003, page 4, lines 7-8) state:

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**"The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and is not conventional in the art. This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art recognized correlation or relationship between the structure of the invention and its function".**

(emphasis added). However, the Applicants' claimed invention describes not solely the method, but also presents detailed description of structural elements such as nucleic acid sequences conserved between multiple organisms and stemloops which are predicted to be indicative of molecular interaction sites, and further provides examples of structures identified by the method which validate the ability of the method to identify the structures. For example, the specification discloses the iron response element (original specification, page 29, lines 3-5, and Example 1) and the Examiner acknowledges that "Since it is known in the art that iron response elements from ferritin mRNAs from different species and human transferrin receptor have a highly conserved six-membered loop...and that this sequence has been demonstrated to be essential (and sufficient) for the translational response to iron..., iron response element is an oligonucleotide comprising a molecular interaction site..." (reference omitted; Office action, July 1, 2003, page 6, lines 8-17). Thus, the specification cites art recognized correlation between the identification of a structure within a molecular interaction site of the invention and the modulation of its function. Additionally, in a previous Office Action mailed June 20, 2002, the Examiner cites Manzella, *et al.*, (J. Biol. Chem., 267, 7077-7082, 1992) and acknowledges that "although Manzella, *et al.*, did not directly disclose that modulation of the expression of ornithine decarboxylase mRNA by binding of a protein [sic] cytoplasmic extracts to ornithine decarboxylase mRNA 5'-UTR..., in the absence of convincing evidence to the contrary, this limitation was considered to be an inherent property." (Office Action, June 20, 2002, page 8, lines 19-21 and bridging to page 9, line 1). Thus, the invention is not described solely in terms of the method used to identify the "molecular interaction sites... wherein the molecular interaction site serves as a binding site for at least one molecule which, when bound to the molecular interaction site, modulates the expression of the RNA in the selected organism,"

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but also presents an example, i.e., Example 1, describing an "art recognized correlation or relationship between the structure of the invention and its function."

Applicants' specification adequately discloses the claimed oligonucleotides comprising molecular interaction sites, and in doing so, also adequately describes relevant, identifying characteristics of the molecular interaction sites. Applicants' specification further teaches that these molecular interaction sites may have secondary structure, (For example, see page 10, lines 27-30; page 23, lines 21-23; page 24, lines 1-2; and Example 3, page 36, lines 17-20 of the original specification as filed), and teaches methods of identifying such molecular interaction sites. Table 1 teaches a list of Exemplary RNA targets containing conserved secondary structured regions, including the "3'-UTR stemloop in vimentin mRNA" (page 11 of original specification), the "3'-UTR of histone mRNA + paralogs" (emphasis added, page 12 of original specification), a region involved in "translational regulation of IL-2" (page 13 of original specification), and the "5'-UTR of ornithine decarboxylase mRNA" (page 14 of original specification). The specification describes in full detail, how, with the histone paralogs in hand, nucleic acid sequences can be aligned to identify conserved regions, and with conserved regions identified, orthologs across species can subsequently be identified through database comparisons which are conventional in the art. Thus, the paralog alignment can be used as a seed sequence "for further sequence similarity searches" (page 22 of original specification). With the paralog alignment in hand, it is conventional in the art to then perform an ortholog search of other taxonomic species, and the specification goes on to describe such an ortholog search which can be used to obtain "at least one sequence region which is conserved among the plurality of nucleic acids from different taxonomic species" (page 23 of original specification). In a subsequent step, the specification describes that "after at least one region that is conserved between the nucleotide sequence of the nucleic acid target and the plurality of nucleic acids from different taxonomic species, preferably via the orthologs, is identified, the conserved region is analyzed to determine whether it contains secondary structure" (page 24). Covariation analysis "for the comparative analysis of RNA structure from sequence alignments" is also described as a means for predicting secondary structure (page 25 of original specification).

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Applicants' specification further describes several examples demonstrating reduction to practice of the claimed method. Page 37 of the specification describes the histone 3'-UTR and a "classic stem-loop structure that has been studied extensively" and this Example goes on to describe how this known structure is used to validate the strategy and methods leading to the claimed oligonucleotides comprising molecular interaction sites. Figure 31 presents an encircled region described as a potentially interesting region of secondary structure, identified by this method, and represents one such oligonucleotide of the claimed invention. Additionally, Example 4 (page 38 of the original specification) describes the highly conserved 3'UTR of vimentin proposed to have a "complex stem-loop structure" and the Applicants' specification goes on to describe that "the same region was identified using the present analysis, thus validating the present approach." Figure 38 also presents two potentially interesting structured regions identified by this method, representing two oligonucleotides of the claimed invention.

The Office Action states that "(w)ith the limited disclosure provided by the specification, the skilled artisan cannot envision all oligonucleotides recited in claims 27-29, 35-41, and 43-67 and therefore conception is not achieved until reduction to practice has occurred." (emphasis added; Office Action, July 1, 2003, page 7, lines 17-19). However, according to the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1 'Written Description' Requirement" 66 Fed. Reg. 1099, 1106 (2001), for a claim drawn to a genus, the written description requirement may be satisfied through a sufficient description of: 1) a representative number of species by actual reduction to practice, 2) reduction to drawings, or 3) disclosure of relevant, identifying characteristics (i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus). Indeed, as described above, Applicants have provided sufficient written description of 1) a representative number of species (for example, the iron response element, 3'-UTR of vimentin and 3'-UTR of histone mRNA), 2) reduction to drawings (Table 1 and Figures 31 and 38, for example) and 3) relevant, identifying characteristics of the claimed invention. Thus, not all oligonucleotides need be envisioned; a representative number of species of said genus are adequately

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described. Applicants believe that the specification discloses the claimed oligonucleotides representing molecular interaction sites identified by the disclosed method, and that one of ordinary skill in the art would understand what is described by the claimed invention and how to carry it out.

The crux of the rejection set forth by the Office appears to be that the present application allegedly does not support "whether there is a molecular interaction site in a region selected from the 3' untranslated regions of histone and vimentin mRNA, and the 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 wherein the molecular interaction site is present in RNAs of at least two different organisms and binding of a molecule to the molecular interaction site modulates the expression of said RNAs in said organisms." (Office Action, July 1, 2003, page 7, lines 2-6). However, a patent applicant's disclosure, which contains a teaching of how to make and use the invention, **must** be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *In re Marzocchi*, 439 F.2d 220, 223-224 (CCPA 1971); *In re Brauna* 34 USPQ2d 1437, 1441 (Fed. Cir.1995). No such reason to doubt the accuracy of Applicants' disclosure was provided. Furthermore, the Revised Interim Guidelines for the Examination of Patent Applications published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp. 71427-71440, cited by the Examiner (Office Action, July 1, 2003, page 4, lines 7-8) also state that "Possession may be shown by actual reduction to practice, or by showing that the invention was **"ready for patenting"** such as by the disclosure of drawings or other descriptions of the invention that are sufficiently specific to enable a person skilled in the art to practice the invention." (emphasis added). Applicants respectfully submit that the absence of working examples "should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement," and "the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970))." (M.P.E.P § 2164.02).

Thus, the Office has not established a *prima facie* case of lack of written description. One having ordinary skill in the art would be able to understand, as well as to make and use the claimed invention using the application as a guide. Therefore, the claims are enabled by the application.

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Applicants cite numerous places in the specification that support written description and enablement. Accordingly, Applicants respectfully request that, in view of these arguments, the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

**IV. The Claims Are Clear and Definite**

Claims 35-41 and 43-67 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Applicants have amended claims 35, 51, 52 and 67 to provide the required antecedent basis. In view of these amendments to the claims, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.



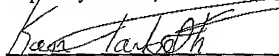
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**V. Conclusion**

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (619) 685-1708 if there are any questions regarding Applicants' claimed invention.

Respectfully submitted,



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